

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
4 January 2001 (04.01.2001)

PCT

(10) International Publication Number
WO 01/00804 A2

(51) International Patent Classification⁷: C12N 15/00

(21) International Application Number: PCT/IB00/00922

(22) International Filing Date: 23 June 2000 (23.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/141,031	25 June 1999 (25.06.1999)	US
60/142,692	1 July 1999 (01.07.1999)	US
199 30 429.7	1 July 1999 (01.07.1999)	DE
199 31 541.8	8 July 1999 (08.07.1999)	DE
199 31 413.6	8 July 1999 (08.07.1999)	DE
199 31 457.8	8 July 1999 (08.07.1999)	DE
199 32 230.9	9 July 1999 (09.07.1999)	DE
199 32 209.0	9 July 1999 (09.07.1999)	DE
199 32 914.1	14 July 1999 (14.07.1999)	DE
60/151,214	27 August 1999 (27.08.1999)	US
199 40 764.9	27 August 1999 (27.08.1999)	DE
199 41 382.7	31 August 1999 (31.08.1999)	DE

(71) Applicant: BASF AKTIENGESSELLSCHAFT
[DE/DE]; D-67056 Ludwigshafen (DE).

(72) Inventors: POMPEJUS, Markus; Wenjenstrasse 21,
D-67251 Freinsheim (DE). KRÖGER, Burkhard; Im
Waldhof 1, D-67117 Limburgerhof (DE). SCHRÖDER,
Hartwig; Goethestrasse 5, D-69226 Nussloch (DE).

ZELDER, Oskar; Rossmarktstrasse 27, D-67346
Speyer (DE). HABERHAUER, Gregor; Moselstrass
42, D-67117 Limburgerhof (DE). LEE, Heung-Shick;
Korea University, Graduate School of Biotechnology,
Anam Dong, Sungbook-Gu, Seoul 136-701 (KR). KIM,
Hyung-Joon; Korea University, Graduate School of
Biotechnology, Anam Dong, Sungbook-Gu, Seoul
136-701 (KR).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— Without international search report and to be republished
upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: *CORYNEBACTERIUM GLUTAMICUM* GENES ENCODING STRESS, RESISTANCE AND TOLERANCE
PROTEINS

(57) Abstract: Isolated nucleic acid molecules, designated SRT nucleic acid molecules, which encode novel SRT proteins from *Corynebacterium glutamicum* are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing SRT nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated SRT proteins, mutated SRT proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of SRT genes in this organism.

What is claimed:

1. An isolated nucleic acid molecule from *Corynebacterium glutamicum* encoding a stress, resistance, or tolerance gene, or a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
2. The isolated nucleic acid molecule of claim 1, wherein said stress, resistance, or tolerance gene is selected from the group consisting of nucleic acid molecules involved in a stress response, tolerance, or resistance to temperature stresses, pH stresses, oxygen stresses, osmotic stresses, toxic chemicals, oxygen radicals, antibiotics, or to lincomycin.
3. An isolated *Corynebacterium glutamicum* nucleic acid molecule selected from the group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, or a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
4. An isolated nucleic acid molecule which encodes a polypeptide sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
5. An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide selected from the group of amino acid sequences consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
6. An isolated nucleic acid molecule comprising a nucleotide sequence which is at least 50% homologous to a nucleotide sequence selected from the group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, or

- 105 -

a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.

- 5 7. An isolated nucleic acid molecule comprising a fragment of at least 15 nucleotides of a nucleic acid comprising a nucleotide sequence selected from the group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
- 10 8. An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule of any one of claims 1-7 under stringent conditions.
- 15 9. An isolated nucleic acid molecule comprising the nucleic acid molecule of any one of claims 1-8 or a portion thereof and a nucleotide sequence encoding a heterologous polypeptide.
10. A vector comprising the nucleic acid molecule of any one of claims 1-9.
- 20 11. The vector of claim 10, which is an expression vector.
12. A host cell transfected with the expression vector of claim 11.
13. The host cell of claim 12, wherein said cell is a microorganism.
- 25 14. The host cell of claim 13, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.
15. The host cell of claim 12, wherein the expression of said nucleic acid molecule results in the modulation in production of a fine chemical from said cell.
- 30 16. The host cell of claim 15, wherein said fine chemical is selected from the group consisting of: organic acids, proteinogenic and nonproteinogenic amino acids, purine

- 106 -

and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

- 5 17. A method of producing a polypeptide comprising culturing the host cell of claim 12 in an appropriate culture medium to, thereby, produce the polypeptide.
18. An isolated stress, resistance, or tolerance polypeptide from *Corynebacterium glutamicum*, or a portion thereof.
- 10 19. The protein of claim 18, wherein said stress, resistance, or tolerance polypeptide is selected from the group consisting of proteins involved in a stress response, tolerance, or resistance to temperature stresses, pH stresses, oxygen stresses, osmotic stresses, toxic chemicals, oxygen radicals, antibiotics, or to lincomycin.
- 15 20. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.
- 20 21. An isolated polypeptide comprising a naturally occurring allelic variant of a polypeptide comprising an amino acid sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, or a portion thereof, provided that the amino acid sequence is not encoded
- 25 by any of the F-designated genes set forth in Table 1.
22. The isolated polypeptide of any of claims 18-21, further comprising heterologous amino acid sequences.
- 30 23. An isolated polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 50% homologous to a nucleic acid selected from the group consisting of those sequences set forth as odd-numbered SEQ ID

NOs of the Sequence Listing,, provided that the nucleic acid molecule does not consist of any of the F-designated nucleic acid molecules set forth in Table 1.

24. An isolated polypeptide comprising an amino acid sequence which is at least 50% homologous to an amino acid sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.

25. A method for producing a fine chemical, comprising culturing a cell containing a vector of claim 12 such that the fine chemical is produced.

26. The method of claim 25, wherein said method further comprises the step of recovering the fine chemical from said culture.

27. The method of claim 25, wherein said method further comprises the step of transfecting said cell with the vector of claim 11 to result in a cell containing said vector.

28. The method of claim 25, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.

29. The method of claim 25, wherein said cell is selected from the group consisting of: *Corynebacterium glutamicum*, *Corynebacterium herculis*, *Corynebacterium lilium*, *Corynebacterium acetoacidophilum*, *Corynebacterium acetoglutamicum*, *Corynebacterium acetophilum*, *Corynebacterium ammoniagenes*, *Corynebacterium fujiokense*, *Corynebacterium nitrilophilus*, *Brevibacterium ammoniagenes*, *Brevibacterium butanicum*, *Brevibacterium divaricatum*, *Brevibacterium flavum*, *Brevibacterium healii*, *Brevibacterium ketoglutamicum*, *Brevibacterium ketosoreductum*, *Brevibacterium lactofermentum*, *Brevibacterium linens*, *Brevibacterium paraffinolyticum*, and those strains set forth in Table 3.

30. The method of claim 25, wherein expression of the nucleic acid molecule from said vector results in modulation of production of said fine chemical.
31. The method of claim 25, wherein said fine chemical is selected from the group
5 consisting of: organic acids, proteinogenic and nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides and enzymes.
- 10 32. The method of claim 25, wherein said fine chemical is an amino acid.
33. The method of claim 32, wherein said amino acid is drawn from the group consisting of: lysine, glutamate, glutamine, alanine, aspartate, glycine, serine, threonine, methionine, cysteine, valine, leucine, isoleucine, arginine, proline, histidine,
15 tyrosine, phenylalanine, and tryptophan.
34. A method for producing a fine chemical, comprising culturing a cell whose genomic DNA has been altered by the inclusion of a nucleic acid molecule of any one of claims 1-9.
- 20 35. A method for diagnosing the presence or activity of *Corynebacterium diphtheriae* in a subject, comprising detecting the presence of one or more SEQ ID NOs 1 through 304 of the Sequence Listing in the subject, provided that the sequences are not or are not encoded by any of the F-designated sequences set forth in Table 1, thereby
25 diagnosing the presence or activity of *Corynebacterium diphtheriae* in the subject.
36. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set forth as odd-numbered SEQ ID NOs of the Sequence Listing, wherein the nucleic acid molecule is disrupted.
- 30 37. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set forth as odd-numbered SEQ ID NOs of the

Sequence Listing , wherein the nucleic acid molecule comprises one or more nucleic acid modifications from the sequence set forth as odd-numbered SEQ ID NOs of the Sequence Listing .

- 5 38. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set as odd-numbered SEQ ID NOs of the Sequence Listing, wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule.

Pro Asp Pro His Gly Thr Asp Leu Val Arg Ala Ala Tyr Val Lys His
435 440 445

Gln Asp Asp Asp Asp Phe Ile Gln Pro Gly Ile Leu Tyr Arg Glu Val
450 455 460

Leu Asp Glu Gly Glu Lys Glu Arg Leu Ala Asp Asn Ile Ser Asn Ala
465 470 475 480

Met Gln Gly Ile Ser Glu Ala Thr Glu Pro Arg Val Tyr Asp Tyr Trp
485 490 495

Asn Asn Val Asp Glu Asn Leu Gly Ala Arg Val Lys Glu Leu Tyr Leu.
500 505 510

Gln Lys Lys Ala
515

<210> 13

<211> 2439

<212> DNA

<213> *Corynebacterium glutamicum*

<220>

<221> CDS

<222> (101)..(2416)

<223> RXA00404

<400> 13

aagatccgat catcggcata cagaaacacc catctggccg aactttcctt tttctgcatg 60

catttctgca cacagtttct gcccgctgtt tctacgcata gtg gct ttg aaa cga 115
Val Ala Leu Lys Arg
1 5

ccc gaa gag aaa aca gta aag atc gtg acc ata aaa cag act gac aac 163
Pro Glu Glu Lys Thr Val Lys Ile Val Thr Ile Lys Gln Thr Asp Asn
10 15 20

atc aat gac gat gat ttg gtg tac agc aac gct act gac ctt cca gta 211
Ile Asn Asp Asp Asp Leu Val Tyr Ser Asn Ala Thr Asp Leu Pro Val
25 30 35

ggc gtg aag aag tcc cct aaa atg tca ccg acc gcc cgc gtt ggt ctc 259
Gly Val Lys Lys Ser Pro Lys Met Ser Pro Thr Ala Arg Val Gly Leu
40 45 50

ctt gtc ttt ggg gtt atc gcg gcg gtg ggt tgg gga gca atc gct ttc 307
Leu Val Phe Gly Val Ile Ala Ala Val Gly Trp Gly Ala Ile Ala Phe
55 60 65

tcc cgt ggc gaa aca atc aac tct gtg tgg ctg gtt ttg gcg gca gtt 355
Ser Arg Gly Glu Thr Ile Asn Ser Val Trp Leu Val Leu Ala Ala Val
70 75 80 85

ggt tcc tat atc att gcg ttt tct ttc tat gcc cga ctg att gaa tac 403
 Gly Ser Tyr Ile Ile Ala Phe Ser Phe Tyr Ala Arg Leu Ile Glu Tyr
 90 95 100

aaa gtt gtt aag ccg aaa gat cag cga gca acc ccg gcg gaa tac gtt 451
 Lys Val Val Lys Pro Lys Asp Gln Arg Ala Thr Pro Ala Glu Tyr Val
 105 110 115

aat gac ggc aag gac tat gtc cca acg gat cgt cgt gtg ctt ttt ggc 499
 Asn Asp Gly Lys Asp Tyr Val Pro Thr Asp Arg Arg Val Leu Phe Gly
 120 125 130

cac cac ttt gca gct att gca ggt gcc ggt cca ttg gtt gga cct gtc 547
 His His Phe Ala Ala Ile Ala Gly Ala Gly Pro Leu Val Gly Pro Val
 135 140 145

atg gcc gcg cag atg ggc tac ctg cca ggc acc ttg tgg att atc ctc 595
 Met Ala Ala Gln Met Gly Tyr Leu Pro Gly Thr Leu Trp Ile Ile Leu
 150 155 160 165

ggt gtg att ttc gcc ggt gca gtg cag gac tac cta gtg ctg tgg gtg 643
 Gly Val Ile Phe Ala Gly Ala Val Gln Asp Tyr Leu Val Leu Trp Val
 170 175 180

tct act cgt agg cgt gga cgc tca ctt ggc cag atg gtt cgt gat gaa 691
 Ser Thr Arg Arg Arg Gly Arg Ser Leu Gly Gln Met Val Arg Asp Glu
 185 190 195

atg ggc acg gtc ggt gga gct gcc ggt atc ttg gcg acc atc tcc atc 739
 Met Gly Thr Val Gly Gly Ala Ala Gly Ile Leu Ala Thr Ile Ser Ile
 200 205 210

atg atc atc att atc gcg gtg ctc gca ttg atc gtg gtt aat gca ctg 787
 Met Ile Ile Ile Ile Ala Val Leu Ala Leu Ile Val Val Asn Ala Leu
 215 220 225

gct gat tca cca tgg ggc gtt ttc tcc atc acc atg acc atc cca att 835
 Ala Asp Ser Pro Trp Gly Val Phe Ser Ile Thr Met Thr Ile Pro Ile
 230 235 240 245

gca ctg ttc atg ggt gtg tac ttg cgt tac ctg cgc cca ggt cgt gtt 883
 Ala Leu Phe Met Gly Val Tyr Leu Arg Tyr Leu Arg Pro Gly Arg Val
 250 255 260

act gaa gtg tcc atc atc ggt gtg gca ctg ctc ctg ctg gct atc gtt 931
 Thr Glu Val Ser Ile Ile Gly Val Ala Leu Leu Leu Leu Ala Ile Val
 265 270 275

gct ggt ggt tgg gtt gca gac acc tca tgg ggc gtg gaa tgg ttc acc 979
 Ala Gly Gly Trp Val Ala Asp Thr Ser Trp Gly Val Glu Trp Phe Thr
 280 285 290

tgg tct aag acc act ttg gcg ttg gcc ttg atc ggt tac gga atc atg 1027
 Trp Ser Lys Thr Thr Leu Ala Leu Ala Leu Ile Gly Tyr Gly Ile Met
 295 300 305

gct gcg att ttg ccg gtg tgg ctg ctg ctt gca ccg cgc gat tac ctg 1075

535	540	545	
ctg cgc cgt ttc aag gat cct tca tgg act gtc ggt aac tgg att tct Leu Arg Arg Phe Lys Asp Pro Ser Trp Thr Val Gly Asn Trp Ile Ser 550 555 560 565			1795
acc gtg ttt gtg tgt gct cta tgg ggt gct att ttg ctc atg ggt gtt Thr Val Phe Val Cys Ala Leu Trp Gly Ala Ile Leu Leu Met Gly Val 570 575 580			1843
acc gat cca ctg ggc ggc atc aac gtg ctt ttc cca cta ttc ggt atc Thr Asp Pro Leu Gly Gly Ile Asn Val Leu Phe Pro Leu Phe Gly Ile 585 590 595			1891
gct aac cag ctg ctc gcc gct att gca ctt gct ctc gtg ctg gtt gtt Ala Asn Gln Leu Leu Ala Ala Ile Ala Leu Ala Leu Val Leu Val Val 600 605 610			1939
gtg gtg aag aag ggc ctg tac aag tgg gcg tgg att cca gct gtt cct Val Val Lys Lys Gly Leu Tyr Lys Trp Ala Trp Ile Pro Ala Val Pro 615 620 625			1987
ttg gca tgg gat ctc att gtc acg atg act gcg tca tgg cag aag att Leu Ala Trp Asp Leu Ile Val Thr Met Thr Ala Ser Trp Gln Lys Ile 630 635 640 645			2035
ttc cac tct gat ccg gct att ggc tac tgg gct cag aac gcg aac ttc Phe His Ser Asp Pro Ala Ile Gly Tyr Trp Ala Gln Asn Ala Asn Phe 650 655 660			2083
cgc gat gca aag tct caa ggc ctt acc gaa ttt ggt gcc gct aaa tct Arg Asp Ala Lys Ser Gln Gly Leu Thr Glu Phe Gly Ala Ala Lys Ser 665 670 675			2131
cct gag gca atc gat gcg gtt atc cga aac acc atg att cag ggc atc Pro Glu Ala Ile Asp Ala Val Ile Arg Asn Thr Met Ile Gln Gly Ile 680 685 690			2179
ttg tcc atc ctg ttc gcg gtg ctc gtc ctc gtt gtt gtc ggc gca gcc Leu Ser Ile Leu Phe Ala Val Leu Val Leu Val Val Val Gly Ala Ala 695 700 705			2227
att gcg gtg tgc atc aag tcc atc agg gct cgt gca gcc gga aca cct Ile Ala Val Cys Ile Lys Ser Ile Arg Ala Arg Ala Ala Gly Thr Pro 710 715 720 725			2275
ttg gag acc act gaa gag cct gat act gaa tct gag ttc ttc gcc cca Leu Glu Thr Thr Glu Glu Pro Asp Thr Glu Ser Glu Phe Phe Ala Pro 730 735 740			2323
act gga ttc ctt gca tct tcc agg gat aag gaa gtc cag gcc atg tgg Thr Gly Phe Leu Ala Ser Ser Arg Asp Lys Glu Val Gln Ala Met Trp 745 750 755			2371
gac gag cgc tac cca ggc ggt gcg ccc gtg tct tct gga ggg cac Asp Glu Arg Tyr Pro Gly Gly Ala Pro Val Ser Ser Gly Gly His 760 765 770			2416

taaaacatga tggctcttac tca

2439

<210> 14

<211> 772

<212> PRT

<213> Corynebacterium glutamicum

<400> 14

Val	Ala	Leu	Lys	Arg	Pro	Glu	Glu	Lys	Thr	Val	Lys	Ile	Val	Thr	Ile
1				5					10					15	

Lys	Gln	Thr	Asp	Asn	Ile	Asn	Asp	Asp	Asp	Leu	Val	Tyr	Ser	Asn	Ala
	20						25						30		

Thr	Asp	Leu	Pro	Val	Gly	Val	Lys	Lys	Ser	Pro	Lys	Met	Ser	Pro	Thr
	35						40					45			

Ala	Arg	Val	Gly	Leu	Leu	Val	Phe	Gly	Val	Ile	Ala	Ala	Val	Gly	Trp
	50					55					60				

Gly	Ala	Ile	Ala	Phe	Ser	Arg	Gly	Glu	Thr	Ile	Asn	Ser	Val	Trp	Leu
65				70						75				80	

Val	Leu	Ala	Ala	Val	Gly	Ser	Tyr	Ile	Ile	Ala	Phe	Ser	Phe	Tyr	Ala
			85						90					95	

Arg	Leu	Ile	Glu	Tyr	Lys	Val	Val	Lys	Pro	Lys	Asp	Gln	Arg	Ala	Thr
		100						105					110		

Pro	Ala	Glu	Tyr	Val	Asn	Asp	Gly	Lys	Asp	Tyr	Val	Pro	Thr	Asp	Arg
	115						120					125			

Arg	Val	Leu	Phe	Gly	His	His	Phe	Ala	Ala	Ile	Ala	Gly	Ala	Gly	Pro
	130					135					140				

Leu	Val	Gly	Pro	Val	Met	Ala	Ala	Gln	Met	Gly	Tyr	Leu	Pro	Gly	Thr
145					150					155					160

Leu	Trp	Ile	Ile	Leu	Gly	Val	Ile	Phe	Ala	Gly	Ala	Val	Gln	Asp	Tyr
			165						170					175	

Leu	Val	Leu	Trp	Val	Ser	Thr	Arg	Arg	Arg	Gly	Arg	Ser	Leu	Gly	Gln
		180						185					190		

Met	Val	Arg	Asp	Glu	Met	Gly	Thr	Val	Gly	Gly	Ala	Ala	Gly	Ile	Leu
	195						200					205			

Ala	Thr	Ile	Ser	Ile	Met	Ile	Ile	Ile	Ile	Ala	Val	Leu	Ala	Leu	Ile
	210					215						220			

Val	Val	Asn	Ala	Leu	Ala	Asp	Ser	Pro	Trp	Gly	Val	Phe	Ser	Ile	Thr
225					230					235					240

Met	Thr	Ile	Pro	Ile	Ala	Leu	Phe	Met	Gly	Val	Tyr	Leu	Arg	Tyr	Leu
				245					250					255	

taaaacatga tggctcttac tca

2439

<210> 14

<211> 772

<212> PRT

<213> Corynebacterium glutamicum

<400> 14

Val	Ala	Leu	Lys	Arg	Pro	Glu	Glu	Lys	Thr	Val	Lys	Ile	Val	Thr	Ile
1			5						10				15		

Lys	Gln	Thr	Asp	Asn	Ile	Asn	Asp	Asp	Asp	Leu	Val	Tyr	Ser	Asn	Ala
			20				25						30		

Thr	Asp	Leu	Pro	Val	Gly	Val	Lys	Lys	Ser	Pro	Lys	Met	Ser	Pro	Thr
		35					40					45			

Ala	Arg	Val	Gly	Leu	Leu	Val	Phe	Gly	Val	Ile	Ala	Ala	Val	Gly	Trp
	50				55						60				

Gly	Ala	Ile	Ala	Phe	Ser	Arg	Gly	Glu	Thr	Ile	Asn	Ser	Val	Trp	Leu
65				70						75				80	

Val	Leu	Ala	Ala	Val	Gly	Ser	Tyr	Ile	Ile	Ala	Phe	Ser	Phe	Tyr	Ala
			85					90					95		

Arg	Leu	Ile	Glu	Tyr	Lys	Val	Val	Lys	Pro	Lys	Asp	Gln	Arg	Ala	Thr
		100						105					110		

Pro	Ala	Glu	Tyr	Val	Asn	Asp	Gly	Lys	Asp	Tyr	Val	Pro	Thr	Asp	Arg
		115					120					125			

Arg	Val	Leu	Phe	Gly	His	His	Phe	Ala	Ala	Ile	Ala	Gly	Ala	Gly	Pro
	130					135					140				

Leu	Val	Gly	Pro	Val	Met	Ala	Ala	Gln	Met	Gly	Tyr	Leu	Pro	Gly	Thr
145				150						155				160	

Leu	Trp	Ile	Ile	Leu	Gly	Val	Ile	Phe	Ala	Gly	Ala	Val	Gln	Asp	Tyr
			165					170						175	

Leu	Val	Leu	Trp	Val	Ser	Thr	Arg	Arg	Arg	Gly	Arg	Ser	Leu	Gly	Gln
		180					185						190		

Met	Val	Arg	Asp	Glu	Met	Gly	Thr	Val	Gly	Gly	Ala	Ala	Gly	Ile	Leu
		195				200					205				

Ala	Thr	Ile	Ser	Ile	Met	Ile	Ile	Ile	Ile	Ala	Val	Leu	Ala	Leu	Ile
	210				215						220				

Val	Val	Asn	Ala	Leu	Ala	Asp	Ser	Pro	Trp	Gly	Val	Phe	Ser	Ile	Thr
225				230						235				240	

Met	Thr	Ile	Pro	Ile	Ala	Leu	Phe	Met	Gly	Val	Tyr	Leu	Arg	Tyr	Leu
			245					250						255	

Arg Pro Gly Arg Val Thr Glu Val Ser Ile Ile Gly Val Ala Leu Leu
 260 265 270
 Leu Leu Ala Ile Val Ala Gly Gly Trp Val Ala Asp Thr Ser Trp Gly
 275 280 285
 Val Glu Trp Phe Thr Trp Ser Lys Thr Thr Leu Ala Leu Ala Leu Ile
 290 295 300
 Gly Tyr Gly Ile Met Ala Ala Ile Leu Pro Val Trp Leu Leu Leu Ala
 305 310 315 320
 Pro Arg Asp Tyr Leu Ser Thr Phe Met Lys Ile Gly Val Ile Gly Leu
 325 330 335
 Leu Ala Val Gly Ile Leu Phe Ala Arg Pro Glu Val Gln Met Pro Ser
 340 345 350
 Val Thr Ser Phe Ala Leu Glu Gly Asn Gly Pro Val Phe Ser Gly Ser
 355 360 365
 Leu Phe Pro Phe Leu Phe Ile Thr Ile Ala Cys Gly Ala Leu Ser Gly
 370 375 380
 Phe His Ala Leu Ile Ser Ser Gly Thr Thr Pro Lys Leu Val Glu Lys
 385 390 395 400
 Glu Ser Gln Met Arg Met Leu Gly Tyr Gly Gly Met Leu Met Glu Ser
 405 410 415
 Phe Val Ala Met Met Ala Leu Ile Thr Ala Val Ile Leu Asp Arg His
 420 425 430
 Leu Tyr Phe Ser Met Asn Ala Pro Leu Ala Leu Thr Gly Gly Asp Pro
 435 440 445
 Ala Thr Ala Ala Glu Trp Val Asn Ser Ile Gly Leu Thr Gly Ala Asp
 450 455 460
 Ile Thr Pro Glu Gln Leu Ser Glu Ala Ala Glu Ser Val Gly Glu Ser
 465 470 475 480
 Thr Val Ile Ser Arg Thr Gly Gly Ala Pro Thr Leu Ala Phe Gly Met
 485 490 495
 Ser Glu Ile Leu Ser Gly Phe Ile Gly Gly Ala Gly Met Lys Ala Phe
 500 505 510
 Trp Tyr His Phe Ala Ile Met Phe Glu Ala Leu Phe Ile Leu Thr Thr
 515 520 525
 Val Asp Ala Gly Thr Arg Val Ala Arg Phe Met Met Thr Asp Thr Leu
 530 535 540
 Gly Asn Val Pro Gly Leu Arg Arg Phe Lys Asp Pro Ser Trp Thr Val
 545 550 555 560

Gly Asn Trp Ile Ser Thr Val Phe Val Cys Ala Leu Trp Gly Ala Ile
 565 570 575
 Leu Leu Met Gly Val Thr Asp Pro Leu Gly Gly Ile Asn Val Leu Phe
 580 585 590
 Pro Leu Phe Gly Ile Ala Asn Gln Leu Leu Ala Ala Ile Ala Leu Ala
 595 600 605
 Leu Val Leu Val Val Val Val Lys Lys Gly Leu Tyr Lys Trp Ala Trp
 610 615 620
 Ile Pro Ala Val Pro Leu Ala Trp Asp Leu Ile Val Thr Met Thr Ala
 625 630 635 640
 Ser Trp Gln Lys Ile Phe His Ser Asp Pro Ala Ile Gly Tyr Trp Ala
 645 650 655
 Gln Asn Ala Asn Phe Arg Asp Ala Lys Ser Gln Gly Leu Thr Glu Phe
 660 665 670
 Gly Ala Ala Lys Ser Pro Glu Ala Ile Asp Ala Val Ile Arg Asn Thr
 675 680 685
 Met Ile Gln Gly Ile Leu Ser Ile Leu Phe Ala Val Leu Val Leu Val
 690 695 700
 Val Val Gly Ala Ala Ile Ala Val Cys Ile Lys Ser Ile Arg Ala Arg
 705 710 715 720
 Ala Ala Gly Thr Pro Leu Glu Thr Thr Glu Glu Pro Asp Thr Glu Ser
 725 730 735
 Glu Phe Phe Ala Pro Thr Gly Phe Leu Ala Ser Ser Arg Asp Lys Glu
 740 745 750
 Val Gln Ala Met Trp Asp Glu Arg Tyr Pro Gly Gly Ala Pro Val Ser
 755 760 765
 Ser Gly Gly His
 770

<210> 15

<211> 255

<212> DNA

<213> Corynebacterium glutamicum

<220>

<221> CDS

<222> (101)..(232)

<223> RXN03119

<400> 15

tgggaggtgt cgcaccaagt acttttgcga agcgccatct gacggatttt caaaagatgt 60

